

Comparative Study on Post Operative Nausea and Vomiting Following Preoperative Administration of Pethidine, Pentazocine and Butorphanol for Intraoperative Analgesia during Gynecological Laparoscopic Surgery

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Abstract

BACKGROUND: Postoperative nausea and vomiting (PONV) is one of the most distressing and common problem following general anaesthesia. Gynaecological laparoscopic procedure and administration of opioids are associated with remarkably high incidence of postoperative nausea and vomiting. Pethidine is a predominantly a mu agonist. Pentazocine is the first opioid agonist-antagonist. Butorphanol is a synthetically mixed opioids agonist- antagonist. This study compared the effect of preoperative administration of pethidine, pentazocine and butorphanol on PONV in young female patients undergoing elective laparoscopic gynecological surgery.

METHOD: In a prospective, randomized, double blind study 90 female patients received equal volume 2ml. of pethidine (50mg), pentazocine (30mg), butorphanol (2mg) by IM route 30 minute before induction. The study groups were similar for patient characteristics; surgical procedure and anesthetic management. Observation was done up to 24 hours postoperatively.

RESULTS: The result of this study showed that the incidence of nausea only in the first 24 hours of the postoperative period was maximum with pethidine and minimum with butorphanol. Even a single episode of vomiting in the first 24 hours of the postoperative period was much higher with pethidine than pentazocine and butorphanol.

CONCLUSION: It may be concluded from this study that incidence of PONV following pre operative Pethidine (50mg), Pentazocine(30mg) and Butorphanol(2mg) is maximum with Pethidine and least with butorphanol.

KEY WORDS: Pethidine, Pentazocine, Butorphanol, PONV.

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I. Introduction

The commonest causes of morbidity after anesthesia and surgery are pain and post operative nausea and vomiting (PONV), (1-3) which are interrelated. Unrelieved pain is a common cause of PONV, and opioids widely used in pain relief are also potent causes of PONV. (4). Uncontrolled PONV may result in dehydration, electrolyte imbalance and aspiration of vomitus. There are also economical implications particularly with increasing practice of day care surgery. The incidence of PONV ranges between 20-30% after general anesthesia (5). Opioids which are considered as the mainstay of pain management cause PONV by direct stimulation of the chemoreceptor trigger zone for emesis, in the area prostroma of the medulla. Nausea and vomiting are less common in patients receiving opioids, who are recumbent, but the incidence increases in ambulatory patients (6,7). This suggests that a vestibular component is also operative. Laparoscopic surgery is also associated with a remarkably high rate of postoperative nausea and vomiting ranging from 20-51% (8,9) of which gynecological one is associated with a little higher rate of PONV between 50-60% (8,9). R.S.J. Clarke in 1989 (10) showed that the opioids are sedative rather than truly anxiolytic, are associated with a high incidence of postoperative nausea and vomiting when used as premedication. Dundee, Loan and Morrison in 1970 (11) found that time of onset of useful effect of most opioids is 40 minutes whereas that with morphine is often delayed until after the operation is over. Sungetal in 1984 (12) in a study comparing butorphanol with morphine, found that patients who received butorphanol had less nausea (8.3% vs. 44.4%) and less vomiting (8.3% vs. 33.3%) than those given morphine. Rowbothom in 1992 (13) suggested that avoidance of the opioids is the most important factor in the prevention of PONV and treatment of PONV is primarily based

on anti emetic therapy and supportive care. In a well designed study, Riding in 1960 (14) demonstrated in patient undergoing endoscopic retrograde cholangio-pancreatography, an increase in PONV from 22.4% in controls to 66.7% in patients receiving premedication with 10mg morphine. The present study was planned to observe the effect of 3 different opioids which are very commonly used for intra and postoperative analgesia on PONV in a group of young female patient undergoing laparoscopic gynecological surgery.

II. Methods

The present study was conducted at Ramakrishna Mission Seva Pratishthan, Kolkata from January,2019 to August,2019. A total number of 90 adult non obese female between 25 to 35 years of age belonging to ASA (American Society of Anaesthesiologists) physical status 1 scheduled for elective laparoscopic gynecological surgery of short duration, under general anaesthesia were recruited in this study. They were randomly allocated into three groups, having 30 patients in each group.

The study conducted was prospective, randomized and double blind.

Group A –inj pethidine Hydrochloride 50mg IV 10 minutes before induction

Group B –inj pentazocine hydrochloride 30 mg IV 10 minutes before induction

Group C –inj butorphanol 2mg IV, 10 minutes before induction.

The study drugs, prepared in identical 2ml syringes were injected through intravascular route, 30 minutes prior to induction of anaesthesia, according to the group they belonged after standard monitors were attached. Each patient received inj Midazolam 0.07mg/kg IV to provide anxiolysis and amnesia. Preoxygenation with 100% oxygen was carried for 3 minutes. Inj glycopyrrolate (0.01mg/kg) was injected followed by intravenous thiopentone (5mg/kg) as inducing agent. Inj atracurium besylate was administered (0.5mg/kg) to facilitate laryngoscopy and intubation. Ventilation was assisted with facemask for 3 minutes followed by laryngoscopy with an appropriate size Macintosh laryngoscope blade and trachea was intubated with a cuffed end tracheal tube of proper size. Anaesthesia was maintained with 66% nitrous oxide in oxygen and intermittent administration of isoflurane and atracurium as and when required. Diclofenac Suppository (100mg) was introduced rectally to facilitate postoperative analgesia. During surgery into abdominal insufflations with carbon dioxide was done and head down position was achieved. The following parameters were monitored intra operatively. Pulse Rate, Systolic, diastolic and mean arterial pressure. ECG in lead II, SaO₂, EtCo₂. At the termination of surgery, patients were made supine, residual neuromuscular blockade was antagonized with neostigmine(0.05mg/kg) and atropine (0.02mg/kg). Trachea was extubated only when all protective reflexes were adequate. All patients were closely monitored in the post anaesthesia care unit for two hours and thereafter in the ward for 24 hours. Supplemental Oxygen (3L/min) was administered through facemask for 4 hours postoperatively. The following parameters were monitored and recorded at 0-2 hours (early post operative period), 2-6 hours (intermediate postoperative period), 6-24 hours (late postoperative period). Antiemetic ondansetron 4mg IV was administered to those patients who vomited once or more and those who complained of nausea or retching lasting for more than 15 minutes. Post operative analgesia was provided to all patients who complained of pain or had a pain score of more than 3 when assessed by a numerical scale. In a 10 cm verbal numerical scale, between 0-10, 0 indicated no pain at all and 10 was considered as worst intolerable pain. Diclofenac sodium 50mg IM was administered to relieve postoperative pain. Incidence of adverse effect if occurred was noted in the post operative period.

All clinical data obtained were tabulated and presented as mean + standard deviation. Demographic parameter tests were compared using ANOVA (Analysis of variance) test. Postoperative parameters like Spo₂ respiratory rate, systolic, diastolic, and mean blood pressure EtCo₂ were compared using ANOVA test. Postoperative nausea and vomiting in three groups were compared using CHI SQUARE test.

P value > 0.05 denotes the difference is not statistically significant.

P value < 0.05 denotes difference is high significant.

P value < 0.01 denotes difference is highly significant.

P value < 0.001 denotes the difference is very highly significant.

III. Results

Ninety patients were included in this study, having 30 patients in each group (n=30). During power analysis α error was set at 5% and β at 2% and a large magnitude of effects (effective size = 0.55) was used to estimate a sufficient sample size. The analysis showed that inclusion of 30 patients per treatment group would be sufficient.

Table 1: Demographic Profile

TABLE 1

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
Age (in Years)	30.93 ± 2.57	30.27 ± 2.7	30.63 ± 2.65	0.33	0.66	0.60
Weight (in Kg)	49.27 ± 4.41	48.8 ± 7.33	49 ± 5.29	0.77	0.83	0.90

TABLE 2: DURATION OF SURGERY AND ANAESTHESIA(IN MINUTES)

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
Duration of Surgery	18.40 ± 0.89	18.43 ± 1.04	18.53 ± 1.01	0.89	0.59	0.71
Duration of Anesthesia	28.90 ± 0.96	28.83 ± 1.09	29.00 ± 1.03	0.80	0.16	0.12

TABLE 3: COMPARISON OF THE INTRA-OPERATIVE HEART RATE (BEATS/MIN) RECORDED AT FIXED INTERVALS

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
At Induction	90.03 ± 9.6	90.33 ± 9.04	88.7 ± 8.47	0.90	0.57	0.47
After 10 Min	89.33 ± 10.38	86.77 ± 9.5	87.63 ± 6.6	0.32	0.45	0.68
After 20 Min	88.47 ± 8.34	87.63 ± 8.74	88.1 ± 5.75	0.71	0.84	0.81

TABLE 4: COMPARISON OF THE INTRA-OPERATIVE ARTERIAL OXYGEN SATURATION (SAO2 IN PERCENTAGE) RECORDED AT FIXED INTERVALS

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
At Induction	96.33 ± 16.32	99.07 ± 0.78	99.2 ± 0.81	0.36	0.34	0.52
After 10 Min	99.47 ± 0.63	99.3 ± 0.65	99.53 ± 0.63	0.32	0.68	0.16
After 20 Min	99.53 ± 0.63	99.3 ± 0.65	99.4 ± 0.72	0.16	0.45	0.58

TABLE 5: COMPARISON OF THE INTRA-OPERATIVE END- TIDAL CO2 CONCENTRATION (MMHG) RECORDED AT FIXED INTERVALS

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
At Induction	32.33 ± 1.84	31.87 ± 1.72	32.33 ± 1.75	0.31	0.99	0.30
After 10 Min	32.37 ± 1.38	32.17 ± 1.98	32.33 ± 1.47	0.65	0.93	0.71
After 20 Min	32.57 ± 1.38	32.67 ± 1.81	32.87 ± 1.48	0.81	0.42	0.64

TABLE 6: COMPARISON OF THE INTRA-OPERATIVE MEAN ARTERIAL PRESSURE RECORDED AT FIXED INTERVALS

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
At Induction	94.24 ± 5.09	95.41 ± 4.09	94.14 ± 5.63	0.33	0.94	0.32
After 10 Min	90.69 ± 5.67	91.71 ± 6.37	91.89 ± 4.91	0.52	0.38	0.90
After 20 Min	88.89 ± 5.92	91.88 ± 6.53	91.09 ± 4.93	0.07	0.12	0.60

TABLE 7: COMPARISON OF THE POST-OPERATIVE MEAN ARTERIAL PRESSURE RECORDED AT FIXED INTERVALS

	A (n = 30)	B (n = 30)	C (n = 30)	P value between Group A and B	P value between Group A and C	P value between Group B and C
After 0 Minutes	91.67 ± 6.32	91.27 ± 5.85	91.29 ± 4.84	0.803	0.797	0.989
After 30 Minutes	91.67 ± 6.14	90.03 ± 6.24	91.09 ± 5.82	0.308	0.708	0.498
After 60 Minutes	91.39 ± 5.87	91.7 ± 6.65	91.92 ± 5.28	0.848	0.715	0.889
After 90 Minutes	90.31 ± 7.18	91.07 ± 6.11	91 ± 5.4	0.659	0.674	0.963
After 120 Minutes	90.41 ± 8.45	91.07 ± 7.44	90.66 ± 5.66	0.747	0.892	0.809

TABLE 8: TABLE SHOWING THE NUMBER OF PATIENTS WHO EXHIBITED NO NAUSEA NO VOMITING DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN B AND C
		A	B	C			
NO NAUSEA/ NO VOMITING	0 to 2 Hours	3 10%	20 27%	24 47%	<0.001	<0.001	0.2375
	2 to 6 Hours	13 43%	21 70%	29 97%			
	6 to 24 Hours	17 57%	26 87%	30 100%	0.006	<0.001	0.032

FIGURE 1

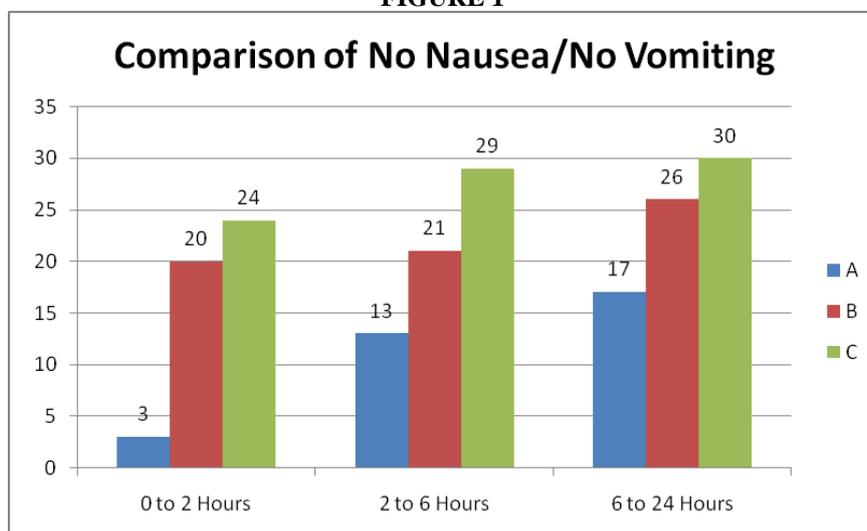


TABLE 9: TABLE SHOWING THE NUMBER OF PATIENTS WHO EXHIBITED NAUSEA BUT NO VOMITING DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN BAND C
		A	B	C			
NAUSEA BUT NO VOMITING	0 to 2 Hours	8	7	5	0.765	0.344	0.517
		27%	23%	16%			
	2 to 6 Hours	11	9	1	0.583	<0.001	0.003
		37%	30%	3%			
	6 to 24 Hours	12	4	0	0.014	<0.001	0.032
		40%	13%	0%			

FIGURE 2

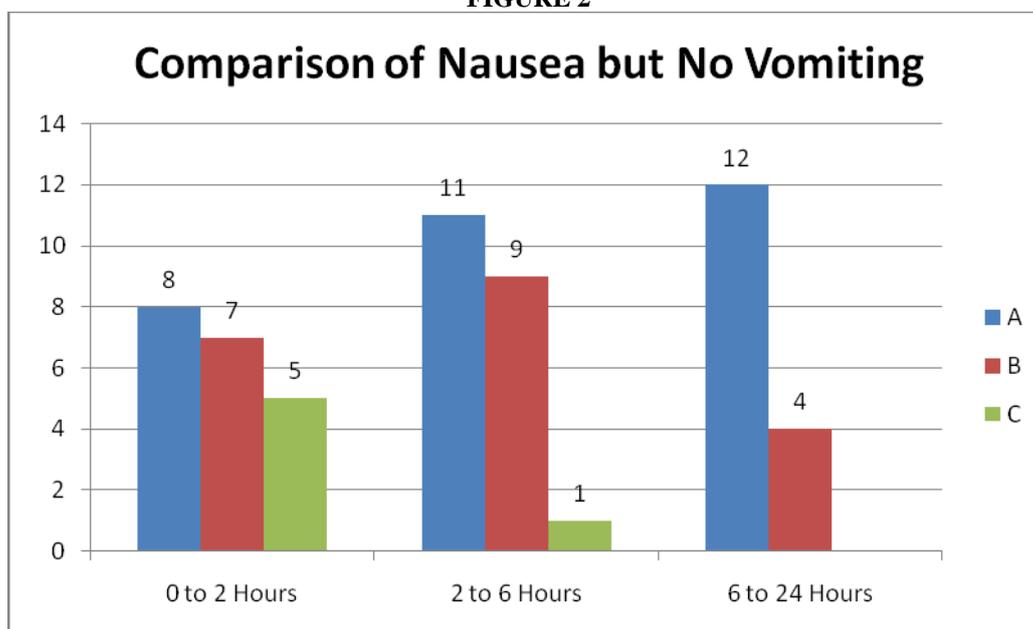


TABLE 10: TABLE SHOWING THE NUMBER OF PATIENTS WHO EXHIBITED ONE EPISODE VOMITING DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN BAND C
		A	B	C			
ONE EPISODE OF VOMITING	0 to 2 Hours	6	3	1	0.273	0.037	0.296
		20%	10%	3%			
	2 to 6 Hours	4	0	0	0.032	0.032	NA#
		13%	0%	0%			
	6 to 24 Hours	1	0	0	0.309	0.309	NA#
		3%	0%	0%			

FIGURE 3

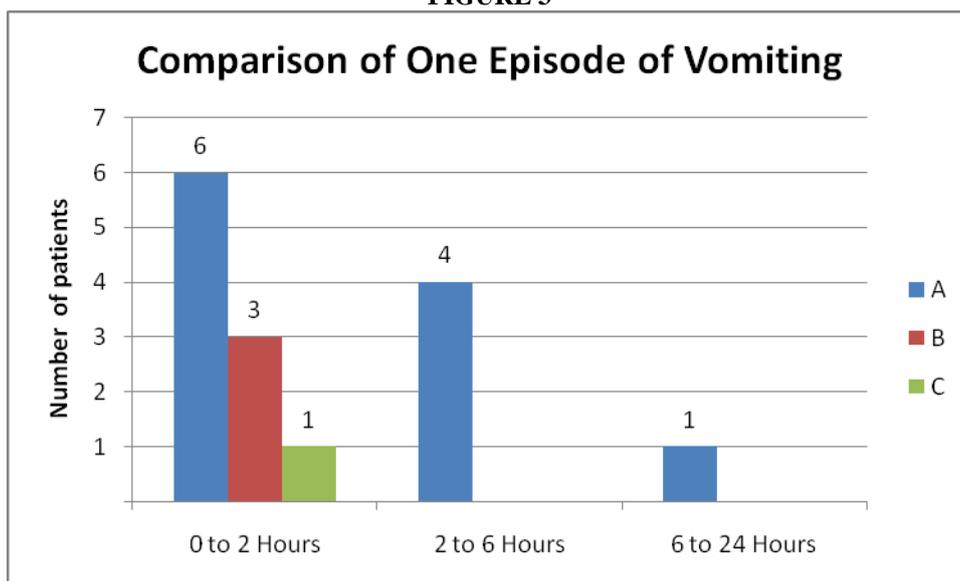


TABLE 11: TABLE SHOWING THE NUMBER OF PATIENTS WHO EXHIBITED TWO EPISODE VOMITING DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN BAND C
		A	B	C			
TWO EPISODE OF VOMITING	0 to 2 Hours	13 43%	0%	0%	<0.001	<0.001	NA#
	2 to 6 Hours	2 7%	0%	0%			
	6 to 24 Hours	0 0%	0%	0%	NA#	NA#	NA#

FIGURE 4

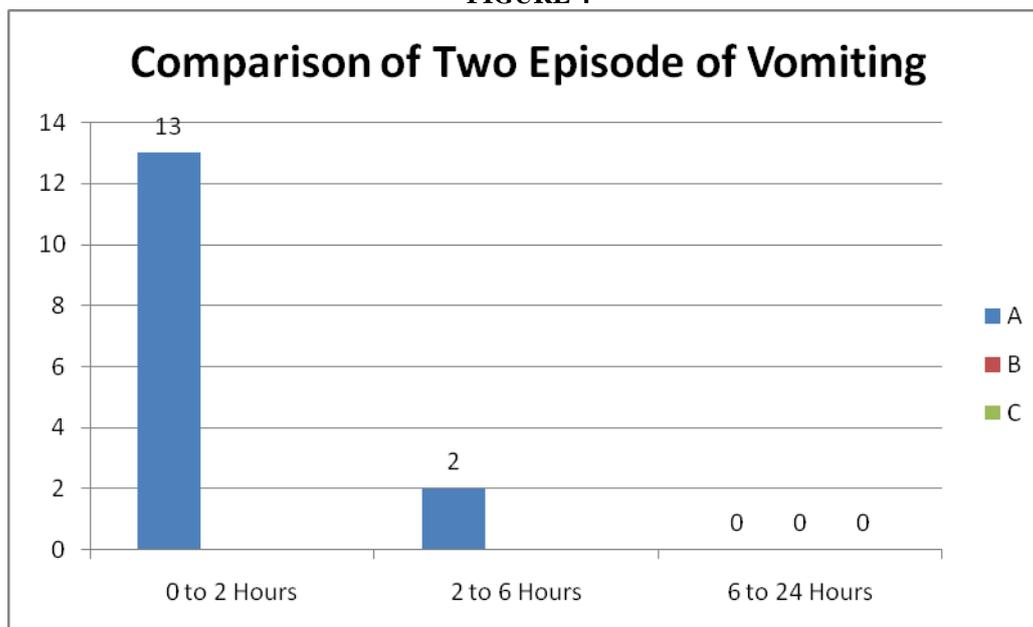


TABLE 12: TABLE SHOWING THE NUMBER OF PATIENTS WHO REQUIRED RESCUE ANTIEMETIC DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN BAND C
		A	B	C			
RESCUE ANTIEMETIC	0 to 2 Hours	19	3	2	<0.001	<0.001	0.640
		63%	10%	7%			
	2 to 6 Hours	6	0	0	0.010	0.010	NA#
		20%	0%	0%			
	6 to 24 Hours	3	0	0	0.076	0.076	NA#
		10%	0%	0%			

TABLE 13: TABLE SHOWING THE NUMBER OF PATIENTS WHO EXHIBITED ADVERSE EFFECTS IN THE POST OPERATIVE PERIOD

Adverse Effects	GROUP		
	A	B	C
CONFUSION	0	0	1
DELIRIUM	3	0	0
MUSCLE RIGIDITY	2	0	0
ORTHOSTATIC HYPOTENSION	1	0	0
PRURISTUS	0	0	2
SEDATION	0	1	0

TABLE 14: TABLE SHOWING THE SCORING OF PATIENTS ON NAUSEA AND VOMITING DURING THE POST OPERATIVE PERIOD RECORDED AT FIXED INTERVAL

		GROUP			P VALUE BETWEEN A AND B	P VALUE BETWEEN A AND C	P VALUE BETWEEN B AND C
		A	B	C			
NAUSEA/ VOMITING SCORE	0 to 2 Hours	1.97±	0.43±	0.27±	<0.001	<0.001	0.290
		1.066	0.679	0.521			
	2 to 6 Hours	0.83±	0.30±	0.03±	0.006	<0.001	0.005
		0.913	0.466	0.183			
	6 to 24 Hours	0.47±	0.13±	0.00±	0.008	<0.001	0.039
		0.571	0.346	0.00			

During the first two post-operative hours, the average nausea- vomiting Score of patients from Group A, Group B and Group C are respectively 1.97, 0.43 and 0.27. The difference between group A and B and group A and C was statistically very significant (p value <0.001), group B and C was not statistically significant (p value 0.290). Between 2 to 6 hours the average nausea- vomiting Score of patients from Group A, Group B and Group C are respectively 0.83, 0.30 and 0.03 The difference between group A and B, group A and C and group B and C was statistically very significant (p value 0.006, <0.001 and 0.005 respectively). Between 6 to 24 hours the average nausea-vomiting Score of patients from Group A, Group B and Group C are respectively 0.47, 0.13 and 0.00 The difference between group A and B and group A and C was statistically very significant (p value 0.008 and <0.001 respectively), while that between and group B and C was statistically significant (p value 0.039).

IV. Discussion

To an anesthesiologist it is not only important to provide a safe and unique course of anesthesia during surgery, but it is also critical to ensure that the post operative course should be free from any discomfort and complications. Postoperative pain and PONV are two major factors which sometimes contribute to significant morbidity. PONV is also common in young female patients undergoing laparoscopy and other gynecological procedures. Patients having any systemic disorder or history of motion sickness were excluded from the study. Vanderberg et al reported that restricting oral intake in the early postoperative period did not decrease the overall incidence of emesis (15). Early fluid intake after emergence from anesthesia in postoperative period leads to increased PONV.(16). Therefore the patients were given oral fluid only after 4 hours of emergence. Pain assessment was done using numerical scoring system. Patients were asked to express their pain in terms of numerical values ranging between 0 and 10. 0 indicates no pain and 10 most severe pain. Patients stating a value of 3 and / or more were considered in need of analgesics and were given diclofenac injection to

relieve their pain. Rescue anti emetics (iv ondansetron 4 mg) were given in each blinded observer's judgment or by patient request. Occurrence of nausea and vomiting were observed for 24 hours postoperatively. For determining the most vulnerable period of PONV, the whole postoperative period was divided into three stages such as early, intermediate and late postoperative period. lasting for 0 to 2, 2 to 6 and 6 to 24 hours respectively. A scoring system was employed to determine the severity of PONV. According to this scoring system

SCORE was **0** when there was NO NAUSEA NO VOMITING

SCORE was **1** when there was ONLY NAUSEA NO VOMITING SCORE **2** was used for ONE EPISODE VOMITING/RETCHING

SCORE **3** was used for TWO OR MORE EPISODES of VOMITING

The emetogenic potential of pentazocine was less than pethidine but more than butorphanol. No statistically significant difference could be appreciated amongst three groups with regard to intra-operative and postoperative vital parameters. There were a few adverse effects in these three groups in the postoperative period. There was delirium (3 patients) muscle rigidity (2 patients) and orthostatic hypotension one patient in group A. There was sedation (1 patient) in group B. In group C two patients had pruritus and one had confusion.

V. Conclusion

It may be concluded from this study that pethidine (50 mg), pentazocine (30mg) and butorphanol (2 mg) given intravascularly 10 minutes prior to induction of anesthesia during short elective gynecological laparoscopic procedures, when supplemented by diclofenac suppository, provide adequate intra-operative analgesia. The incidence and severity of postoperative nausea and vomiting was remarkably high with pethidine with increased need for antiemetic injections. PONV was comparatively less with butorphanol both in incidence and severity. Incidence and severity of PONV after pentazocine was less than pethidine but it was more than butorphanol.

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CONFLICT OF INTEREST: None declared

ETHICS APPROVAL: The study was approved by the Institutional Ethics Committee of the institute where study was conducted.

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